Plasticity workshop:
Neuronal plasticity in the olfactory bulb during simple and complex learning

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Olfactory system
Olfactory system
Olfactory system

Higher order olfactory centers

Olfactory epithelium

Olfactory bulb

OSN

Gl

M

PG

Gr

Image of olfactory epithelium

Image of olfactory bulb

Diagram showing the olfactory system with labeled structures.
Olfactory system

Higher order olfactory centers

OSN

Olfactory epithelium

Olfactory bulb
Olfactory system

Buck and Axel, Cell, 1991; Duchamp-Viret et al., Science, 1999; Shepherd, Physiol Rev, 1972
Adult neurogenesis is a process dependent on sensory experiences.

Lledo et al. Nat Neuro 2006; Rocherfort et al. J Neuro 2002; Mandairon et al. Behav Neuro, 2006; Mandairon et al., J Neuro, 2011; Alonso et al., J Neuro, 2006; Moreno et al., PNAS, 2009
Adult neurogenesis

LONG-TERM FATE AND DISTRIBUTION OF NEWBORN CELLS IN THE ADULT MOUSE OLFACTORY BULB: INFLUENCES OF OLFACTORY DEPRIVATION

N. Mandairon, J. Sacquet, F. Jourdan and A. Didier

Cellular and Behavioral Effects of Cranial Irradiation of the Subventricular Zone in Adult Mice

Françoise Lazarini, Marc-André Mouthon, Gilles Gheusi, Fabrice de Chaumont, Jean-Christophe Olivo-Marin, Stéphanie Lamarque, Djohar Nora Abrous, François D. Boussin, and Pierre-Marie Lledo

Enriched Odor Exposure Increases the Number of Newborn Neurons in the Adult Olfactory Bulb and Improves Odor Memory

Christelle Rochefort, Gilles Gheusi, Jean-Didier Vincent, and Pierre-Marie Lledo

<table>
<thead>
<tr>
<th>Olfactory enrichment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lavender</td>
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<tr>
<td>Garlic</td>
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<tr>
<td>Paprika</td>
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<tr>
<td>Marjoram</td>
</tr>
<tr>
<td>Curry</td>
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<tr>
<td>Rosemary</td>
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<tr>
<td>Nutmeg</td>
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<tr>
<td>Thyme</td>
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<tr>
<td>Basil leaves</td>
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<tr>
<td>Cumin</td>
</tr>
<tr>
<td>Cardamom</td>
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<tr>
<td>Tarragon</td>
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<tr>
<td>Whole cloves</td>
</tr>
<tr>
<td>Chocolate</td>
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<tr>
<td>Celery</td>
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<tr>
<td>Anise</td>
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<tr>
<td>Ginger</td>
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<tr>
<td>Lemon</td>
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<tr>
<td>Orange</td>
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<tr>
<td>Banana</td>
</tr>
</tbody>
</table>

Activation of adult-born neurons facilitates learning and memory

Mariana Alonso, Gabriel Lepouse, Sebastien Wagner, Cedric Bardy, Marie-Madeleine Gabellec, Nicolas Torquet, and Pierre-Marie Lledo

Olfactory perceptual learning requires adult neurogenesis

Mélimisa M. Moreno, Christiane Linster, Olga Espanilla, Joëlle Sacquet, Anne Didier, and Nathalie Mandairon

AraC

In vivo
Perceptual learning

Significant improvement of the discrimination abilities of perceptually close odorants after repeated exposition to these same odorants (= enrichment).

Moreno et al., PNAS, 2009
Moreno et al., J Neuro, 2012

1h/day
For 10 days

No discrimination

Discrimination

Investigation time (s)

hab1 hab2 hab3 hab4 test

Investigation time (s)

hab1 hab2 hab3 hab4 test
Perceptual learning ...

... specifically improve discrimination of learned odorants

... is associated with an increased density of newborn neurons in the granular cell layer ...

... newborn neurons whose contribution to odor processing is increased ...

... and newborn neurons who are necessary for this learning task.

Moreno et al., PNAS, 2009
• Simple perceptual learning paradigm = 1 pair of odorants

• Real olfactory environnement is more complexe = several pairs of odorants
Neuronal plasticity in the olfactory bulb during simple and complex learning

1 - Discrimination performances of every couple of odorants

2 - Neurogenic correlate: newborn neurons density (BrdU) and cellular activity in response to the learned odorants (Zif268)

3 - Structural plasticity and specificity of newborn neurons: study of newborn neurons changing morphological traits as opposed to what happens in preexisting neurons
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**1 - Behavior:**

**TEST ODORANT**

- **NE: NON-ENRICHED**
  - +LIM/-LIM
    - Investigation time (s)
      - hab1: n/a
      - hab2: n/a
      - hab3: n/a
      - hab4: n/a
      - test: n/a
    - ***

- **GROUP 1: +LIM/-LIM ENRICHED**
  - Investigation time (s)
    - hab1: n/a
    - hab2: n/a
    - hab3: n/a
    - hab4: n/a
    - test: n/a
  - ***

- **GROUP 2: +LIM/-LIM & DEC/DODEC ENRICHED**
  - Investigation time (s)
    - hab1: n/a
    - hab2: n/a
    - hab3: n/a
    - hab4: n/a
    - test: n/a
  - ***

**DEC/DODEC**

- +LIM/-LIM
  - Investigation time (s)
    - hab1: n/a
    - hab2: n/a
    - hab3: n/a
    - hab4: n/a
    - test: n/a
  - ***

- GROUP 1: +LIM/-LIM ENRICHED
  - Investigation time (s)
    - hab1: n/a
    - hab2: n/a
    - hab3: n/a
    - hab4: n/a
    - test: n/a
  - ***

- GROUP 2: +LIM/-LIM & DEC/DODEC ENRICHED
  - Investigation time (s)
    - hab1: n/a
    - hab2: n/a
    - hab3: n/a
    - hab4: n/a
    - test: n/a
  - ***

- *** vs. ns
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2 - Newborn neurons density:

![Image of newborn neurons](image_url)

![Graph showing density of BrdU-positive cells](graph_url)
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2 - Newborn neurons responsiveness:

Zif+ neuron

Zif- neuron

![Images of DAPI, GFP, Zif268, and Merged images for Zif+ and Zif- neurons]

![Bar graph showing BrdU+/Zif268+/NeuN+ cells (%) for different groups: NE, NE Group 1, NE Group 2.](Image)
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3 - Newborn neurons and preexisting neurons morphology:

Modified from Kelsh et al. 2009
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Modified from Kelsh et al. 2009
Neuronal plasticity in the olfactory bulb during simple and complex learning

Modified from Kelsh et al. 2009
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Basal spine density

Apical spine density

Modified from Kelsh et al. 2009

Basal domain

Apical domain
Neuronal plasticity in the olfactory bulb during simple and complex learning

Automated reconstruction of three-dimensional neuronal morphology from laser scanning microscopy images

Alfredo Rodriguez,\textsuperscript{a,b} Douglas Ehlenberger,\textsuperscript{a,b} Kevin Kelliher,\textsuperscript{a,b} Michael Einstein,\textsuperscript{a,c,d} Scott C. Henderson,\textsuperscript{a,c,f} John H. Morrison,\textsuperscript{a,c,d,f} Patrick R. Hof,\textsuperscript{a,c,d,f} and Susan L. Wearne\textsuperscript{a,b,d,f,*}
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3a – Newborn neurons

**Arborization length (μm)**

- NE
- Group 1
- Group 2

**Primary dendrite length (μm)**

- NE
- Group 1
- Group 2

**Basal dendrites length (μm)**

- NE
- Group 1
- Group 2

**Apical spines density (spines/μm)**

- NE
- Group 1
- Group 2

**Basal spines density (spines/μm)**

- NE
- Group 1
- Group 2

*Significant differences indicated by asterisks:*
- ***: p < 0.001
- #: p < 0.05
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**Apical spines density (spines/μm)**

- NE
- Group 1
- Group 2

**Basal spines density (spines/μm)**

- NE
- Group 1
- Group 2
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3b – Preexisting neurons

**Arborization length (µm)**

- NE
- Group 1
- Group 2

**Apical spines density (spines/µm)**

- NE
- Group 1
- Group 2

**Primary dendrite length (µm)**

- NE
- Group 1
- Group 2

**Basal spines density (spines/µm)**

- NE
- Group 1
- Group 2

**Basal dendrites length (µm)**

- NE
- Group 1
- Group 2
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Conclusion

Perceptual learning is associated with:

- Increased survival of newborn neurons independently of learning complexity
- Increased recruitment of newborn neurons to the processing of the learned odorants
- Increased spines density at the apical and basal domains of newborn neurons
- No morphological modifications of preexisting neurons
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**Hypothesis:**

↑ inhibition on mitral
↓ overlap of odorants patterns

**Behavior:**

↑ discrimination

↑ spine density = spine density

↑ responsiveness = spine density

**Conclusion**

Before learning

After learning
CRNL - Neuropop Team:
- Anne Didier
- Nathalie Mandairon
- Marion Richard
- Nicola Kuczewski
- Joelle Sacquet
- Maellie Midroit
- Xuming Yin
- Claire Terrier